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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GODDARD, LAURA B	
ART UNIT	**PAPER NUMBER**
1642	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/621,269	THORPE ET AL.	
	Examiner	Art Unit	
	Laura B. Goddard, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,23,51,52 and 93-122* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19,23,51,52 and 93-122* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/7/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed October 16, 2006 in response to the Office Action of April 7, 2006, is acknowledged and has been entered. Previously pending claims 1, 9-12, 93, 94, 96, and 97 have been amended. New claims 100-122 are added. Claims 1-19, 23, 51, 52, and 93-122 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Specification

3. The amendment filed 10/16/2006 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: All of the amendments proposed for the specification filed 10/16/2006 with regards to antibodies that are not 3G4. Although Applicants do not appear to specifically point to any declaration or experimental support for the new property of the antibodies disclosed in the amendments to the specification, Applicants submitted an IDS on 12/7/2006 that included the Ran et al (Clinical Cancer Research, 2005, 11:1551-1562) and Luster et al (J of Biological Chemistry, 2006) journal articles that teach antibody 3G4 is serum-dependent and requires the presence of a protein cofactor to bind phosphatidylserine. The specification originally disclosed that antibody 3G4 and other antibodies were

serum-independent. While these journal articles support the proposed amendments of serum-dependence for deposited antibody 3G4 as a newly discovered, inherent characteristic of antibody 3G4, the articles do not support the amendments to the specification for changing the binding properties of antibodies other than 3G4.

Applicant is required to cancel the new matter in the reply to this Office Action.

NEW REJECTIONS

(necessitated by amendments)

Claim Rejections - 35 USC § 112

4. Claims 1-19, 23, 51, 52, 93-104, 107-110, 113-115, 118-120, and 122 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation wherein said "**antibody binds to phosphatidylserine and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidylserine**", "**that binds to substantially the same epitope as the monoclonal antibody 3G4**", and "**wherein said antibody binds to phosphatidylserine in combination with a protein cofactor**" has no clear support in the specification and the claims as originally filed. THIS IS A NEW MATTER REJECTION.

Applicants amended the specification on 10/16/2006 to change a property disclosed of the deposited and published antibodies in Tables 2 and 4. The amendments changed the antibodies from being serum-independent to being serum-

dependent. Antibody 3G4 was previously thought to bind phosphatidylserine without binding to a protein cofactor or serum protein, however, Applicants later realized this was not correct. Applicants point to their specification amendments filed 10/16/2006 to support the newly added claims or claim limitation. The limitation "antibody binds to phosphatidylserine and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidylserine" now encompasses a broader spectrum of antibodies that bind to phosphatidylserine and any, unidentified protein cofactor, as opposed to binding to a single 3G4 epitope on phosphatidylserine only as originally disclosed by Applicants. The claims broaden the scope of the invention as originally disclosed in the specification. The claim limitation "wherein said antibody binds to phosphatidylserine in combination with a protein cofactor" also broadens the scope of the invention as originally disclosed in the specification for similar reasoning. The claim limitation an stating an antibody "**that binds to substantially the same epitope as the monoclonal antibody 3G4"** also broadens the scope of the invention as now comprising antibodies that bind to both phosphatidylserine and a protein cofactor, because Applicants discovered antibody 3G4 binds to both phosphatidylserine and a protein cofactor, not to phosphatidylserine alone as originally disclosed. Applicants deposited antibody 3G4 at the time of filing and have support to change the epitope or binding property of the deposited antibody that they were in possession of at the time of filing, however, Applicants do not have support for and were not in possession of all other antibodies that compete for binding with 3G4, bind to phosphatidylserine in combination with any protein cofactor, or antibodies that bind to substantially the same epitope as 3G4 as

originally filed because Applicants have changed the epitope and binding properties of 3G4 as originally filed. The deposit of 3G4 supports only changes in the disclosure of the 3G4 epitope and binding properties of 3G4 itself, and does not support changes in the epitopes and binding properties of all other claimed antibodies as stated above.

5. Claims 100, 108, 113, and 118 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection.

The claims are drawn to an **antibody** that binds to phosphatidylserine in combination with a **protein cofactor**.

The amended specification discloses non-limiting examples of protein cofactors or serum proteins such as β_2-glycoprotein I, prothrombin kininogens, prekallikakrein and factor XI. The pathogenic anti-phospholipid antibodies circulating in patients with antiphospholipid syndrome are believed to bind phosphatidylserine, phosphatidylethanolamine and other phospholipids in combination with serum proteins (10/16/2006 specification amendment, p. 202, lines 24 to p. 203, line 2). The specification discloses serum-dependent monoclonal antibodies in Table 2 (see amendment to the specification filed 10/16/2006). The specification does not disclose

any other **protein cofactors** or **antibodies** that bind to phosphatidylserine in combination with **any protein cofactor** as broadly encompassed in the claims.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation of "binds to phosphatidylserine in combination with a protein cofactor". Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that " [a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name', of the claimed subject matter sufficient to distinguish it from other materials. " Id. At 1567, 43 USPQ2d at 1405. The court also stated that:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not

> specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such

characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. Thus, the instant specification may provide an adequate written description of an antibody that binds to phosphatidylserine in combination with a protein cofactor, per Lilly by structurally describing representative protein cofactors or specific antibodies or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not directly describe an antibody that binds to phosphatidylserine in combination with a protein cofactor useful in the claimed invention in a manner that satisfies either the Lilly or Enzo standards. Although the specification discloses monoclonal antibodies that are serum-dependent (Table 2) and non-limiting examples of protein cofactors, this does not provide a description of the broadly claimed antibodies that bind to phosphatidylserine in combination with a protein cofactor that would satisfy the standard set out in Enzo because the specification provides no functional characteristics coupled to structural features.

Further, the specification also fails to describe an antibody that binds to phosphatidylserine in combination with a protein cofactor by the test set out in Lilly because the specification describes only specific monoclonal antibodies that are serum-dependent and non-limiting examples of protein cofactors. Therefore it necessarily fails to describe a representative number of such species.

Thus, the specification does not provide an adequate written description of an antibody that binds to phosphatidylserine in combination with a protein cofactor that is required to practice the claimed invention.

Further, the following teaching of the court as set out in Noelle also clearly applies to the instant claimed invention. The court teaches as follows: "Noelle did not provide sufficient support for the claims to the human CD40CR antibody in his '480 application because Noelle failed to disclose the structural elements of human CD40CR antibody or antigen in his earlier '799 application. Noelle argues that because antibodies are defined by their binding affinity to antigens, not their physical structure, he sufficiently described human CD40CR antibody by stating that it binds to human CD40CR antigen. Noelle cites Enzo Biochem II for this proposition. This argument fails, however, because Noelle did not sufficiently describe the human CD40CR antigen at the time of the filing of the '799 patent application. In fact, Noelle only described the mouse antigen when he claimed the mouse, human, and genus forms of CD40CR antibodies by citing to the ATCC number of the hybridoma secreting the mouse CD40CR antibody. If Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed its antibody by simply stating its binding affinity for the

"fully characterized" antigen. Noelle did not describe human CD40CR antigen. Therefore, Noelle attempted to define an unknown by its binding affinity to another unknown. As a result, Noelle's claims to human forms of CD40CR antibody found in his '480 application cannot gain the benefit of the earlier filing date of his '799 patent application. Moreover, Noelle cannot claim the genus form of CD40CR antibody by simply describing mouse CD40CR antigen". *Randolph J. Noelle v Seth Lederman, Leonard Chess and Michael J. Yellin* (CAFC, 02-1187, 1/20/2004).

In the instant application, the specification only discloses specific serum-dependent monoclonal antibodies and non-limiting examples of structurally different protein cofactors. The instant application does not however fully describe the antibody that binds to phosphatidylserine in combination with a protein cofactor or the protein cofactor. While the structure of phosphatidylserine is known and adequately described, the full scope of epitopes and antigens comprising both phosphatidylserine and any protein cofactor has not been adequately described to describe the antibodies binding to them. Since the instant application does not fully describe the genus of antigen to which the claimed monoclonal antibody binds, the instant application cannot claim the genus form of antibody by simply describing the antigen as a phosphatidylserine in combination with a protein cofactor. Thus the specification fails to describe the claimed antibody, by the test set out in the example of Noelle.

NEW REJECTIONS

(based on new considerations)

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claim 95 is rejected under 35 U.S.C. 101 because the claimed invention, an antibody, is directed to non-statutory subject matter.

The claim reads on an antibody that is found in nature. Products of nature do not constitute patentable subject matter as defined in 35 USC 101. See MPEP 2105. Since an antibody does not exist in nature in purified form, it is suggested that Applicant use the language "isolated" or "purified" in connection with the antibody to identify a product that is found in nature.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 95 and 122 are rejected under 35 U.S.C. 102(b) as being anticipated by Maneta-Peyret et al (J of Immunological Methods, 1988, 108:123-127).

The claims are drawn to an antibody that binds to phosphatidylserine and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidylserine, wherein said antibody is prepared by a process comprising immunizing an animal with activated endothelial cells (claim 95) and a composition comprising a purified antibody, wherein said antibody binds to phosphatidylserine and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidylserine (claim 122).

Maneta-Peyret et al teach a polyclonal antibodies that bind to phosphatidylserine (see pages 124-127; Figure 3; abstract). It would be expected that a subset of the polyclonal antibodies taught by Maneta-Peyret et al would effectively compete with antibody 3G4 for binding to phosphatidylserine, hence all of the limitations of the claims are met.

Although the reference does not specifically state that the antibody can be produced by immunizing an animal with activated endothelial cells, the production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art. Therefore, even if a particular process used to prepare a product is novel and unobvious over the prior art, the product per se, even when limited to the particular process, is unpatentable over the same product taught by the prior art. See In re Kind, 207 F.2d 618, 620, 43 USPQ 400, 402 (CCPA 1939); In re Merz, 97 F.2d 599, 601, 38 USPQ 143, 144-145 (CCPA 1938); In re Bergy, 563 F.2d 1031, 1035, 195 USPQ 344, 348 (CCPA 1977) *vacated* 438 U.S. 902 (1978);

and United States v. Ciba-Geigy Corp., 508 F. Supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979).

8. Claims 1-6, 12, 23, 93-98, 101, 102, 109, 110, 114, 115, 119, 120 and 122 are rejected under 35 U.S.C. 102(b) as being anticipated by Rote et al (Clinical immunology and Immunopathology, 1993, 66:193-200).

The claims are drawn to a composition comprising a purified monoclonal antibody that binds to phosphatidylserine and effectively competes with monoclonal antibody 3G4 for binding to phosphatidylserine (claim 1), wherein said antibody further binds to phosphatidic acid and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidic acid (claim 2), wherein said antibody further binds to phosphatidylinositol and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidylinositol (claim 3), wherein said antibody further binds to phosphatidylglycerol and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidylglycerol (claim 4), wherein said antibody further binds to cardiolipin and effectively competes with the monoclonal antibody 3G4 for binding to cardiolipin (claim 5), the composition of claim 1 wherein said antibody further binds to phosphatidic acid, phosphatidylinositol, phosphatidylglycerol, and cardiolipin and effectively competes with the monoclonal antibody 3G4 for binding to each said aminophospholipids (claim 6), the composition of claim 1, wherein said antibody is an IgM antibody (claim 12), the composition of claim 1 wherein said antibody is prepared

by a process comprising immunizing an animal with activated cells (claim 23), a composition comprising a monoclonal antibody that binds to substantially the same epitope as 3G4 (claim 93), a composition comprising a purified monoclonal antibody that binds to phosphatidylserine and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidylserine (claim 94), an antibody that binds to phosphatidylserine and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidylserine, wherein said antibody is prepared by a process comprising immunizing an animal with activated endothelial cells (claim 95), a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a purified monoclonal antibody that binds to phosphatidylserine and effectively competes with monoclonal antibody 3G4 for binding to phosphatidylserine (claim 96), a purified monoclonal antibody that binds to phosphatidylserine and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidylserine (claim 97), a hybridoma that produces a monoclonal antibody that effectively competes with the monoclonal antibody 3G4 for binding to phosphatidylserine (claim 98), the antibody of claim 1, 96, 97, 98 wherein said antibody binds to PS in an ELISA with blocking buffer comprising 10% bovine serum (claims 101, 102, 109, 110, 114, 115, 119, 120), a composition comprising a purified antibody that binds to phosphatidylserine and effectively competes with monoclonal antibody 3G4 for binding to phosphatidylserine (claim 122).

Rote et al teach a purified monoclonal IgM antibody BA3B5C4 (referred to in the specification as "BA3") and 3Sb9b (referred to in the specification as "3SB"), both of which bind to phosphatidylserine, phosphatidic acid, phosphatidylinositol,

phosphatidylglycerol, and cardiolipin (p. 195; Fig. 1). The antibodies are comprised in a pharmaceutically acceptable carrier, PBS (p. 194, col. 1 and 2). Rote et al teach an ELISA wherein bovine serum (FBS) was used for blocking (p. 194, col. 1). Rote et al teach hybridomas producing the monoclonal antibodies (p. 194, col. 1).

The reference does not specifically teach that the monoclonal antibody effectively competes with 3G4, binds to substantially the same epitope as 3G4, or binds to PS in an ELISA that comprises blocking buffer comprising 10% bovine serum. However, the claimed monoclonal antibody appears to be the same as the prior art antibody, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Although the reference does not specifically state that the antibody can be produced by immunizing an animal with activated endothelial cells, the production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art. Therefore, even if a particular process used to prepare a product is novel and unobvious over the prior art, the product per se, even when limited to the particular process, is unpatentable over the same product taught by the prior art. See In re Kind, 207 F.2d 618, 620, 43 USPQ 400, 402 (CCPA

1939); In re Merz, 97 F.2d 599, 601, 38 USPQ 143, 144-145 (CCPA 1938); In re Bergy, 563 F.2d 1031, 1035, 195 USPQ 344, 348 (CCPA 1977) *vacated* 438 U.S. 902 (1978); and United States v. Ciba-Geigy Corp., 508 F. Supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979).

9. Claims 1, 2, 5, 12, 13, 23, 93-97, 101, 102, 109, 110, 114, 115, 119, 120 and 122 are rejected under 35 U.S.C. 102(b) as being anticipated by Umeda et al (J of Immunology, 1989, 143:2273-2279).

The claims are drawn to a composition comprising a purified monoclonal antibody that binds to phosphatidylserine and effectively competes with monoclonal antibody 3G4 for binding to phosphatidylserine (claim 1), wherein said antibody further binds to phosphatidic acid and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidic acid (claim 2), wherein said antibody further binds to cardiolipin and effectively competes with the monoclonal antibody 3G4 for binding to cardiolipin (claim 5), wherein said antibody is an IgM antibody (claim 12), wherein said antibody is an IgG antibody (claim 13), the composition of claim 1 wherein said antibody is prepared by a process comprising immunizing an animal with activated cells (claim 23), a composition comprising a monoclonal antibody that binds to substantially the same epitope as 3G4 (claim 93), a composition comprising a purified monoclonal antibody that binds to phosphatidylserine and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidylserine (claim 94), an antibody that binds to

phosphatidylserine and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidylserine, wherein said antibody is prepared by a process comprising immunizing an animal with activated endothelial cells (claim 95), a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a purified monoclonal antibody that binds to phosphatidylserine and effectively competes with monoclonal antibody 3G4 for binding to phosphatidylserine (claim 96), a purified monoclonal antibody that binds to phosphatidylserine and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidylserine (claim 97), the antibody of claim 1, 96, 97, 98 wherein said antibody binds to PS in an ELISA with blocking buffer comprising 10% bovine serum (claims 101, 102, 109, 110, 114, 115, 119, 120), a composition comprising a purified monoclonal antibody that binds to phosphatidylserine and effectively competes with monoclonal antibody 3G4 for binding to phosphatidylserine (claim 122).

Umeda et al teach IgM monoclonal antibodies PS4A7, PS3A, PSC8, the IgG monoclonal antibody PS1G3, and monoclonal antibodies PS2C11, PSF10, and PS1B, all of which bind phosphatidylserine and some of which bind to phosphatidic acid (PS4A7, PS1G3, PSC8, PS2C11, PSF10, PS1B) and cardiolipin (PS1G3, PSC8, PSF10, PS1B) (p. 2275, both columns; Fig. 2 and 3). Umeda teach an ELISA wherein the wells are blocked with bovine serum (BSA) (p. 2274, col. 2). Umeda et al teach the antibodies were comprised in a pharmaceutically acceptable carrier (p. 2274, col. 2).

The reference does not specifically teach that the monoclonal antibody effectively competes with 3G4, binds to substantially the same epitope as 3G4, or binds to PS in

an ELISA that comprises blocking buffer comprising 10% bovine serum. However, the claimed monoclonal antibody appears to be the same as the prior art antibody, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Although the reference does not specifically state that the antibody can be produced by immunizing an animal with activated endothelial cells, the production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art. Therefore, even if a particular process used to prepare a product is novel and unobvious over the prior art, the product per se, even when limited to the particular process, is unpatentable over the same product taught by the prior art. See In re Kind, 207 F.2d 618, 620, 43 USPQ 400, 402 (CCPA 1939); In re Merz, 97 F.2d 599, 601, 38 USPQ 143, 144-145 (CCPA 1938); In re Bergy, 563 F.2d 1031, 1035, 195 USPQ 344, 348 (CCPA 1977) *vacated* 438 U.S. 902 (1978); and United States v. Ciba-Geigy Corp., 508 F. Supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979).

10. Claims 1-8, 12-19, 51, 52, 93, 94, 96, 97, 98, 100-102, 108-110, 113-115, 118-120, and 122 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/02584, Thorpe and Ran, published 1/20/2000, IDS.

The claims are drawn to a composition comprising a purified monoclonal antibody that binds to phosphatidylserine and effectively competes with monoclonal antibody 3G4 for binding to phosphatidylserine (claim 1), wherein said antibody further binds to phosphatidic acid and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidic acid (claim 2), wherein said antibody further binds to phosphatidylinositol and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidylinositol (claim 3), wherein said antibody further binds to phosphatidylglycerol and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidylglycerol (claim 4), wherein said antibody further binds to cardiolipin and effectively competes with the monoclonal antibody 3G4 for binding to cardiolipin (claim 5), the composition of claim 1 wherein said antibody further binds to phosphatidic acid, phosphatidylinositol, phosphatidylglycerol, and cardiolipin and effectively competes with the monoclonal antibody 3G4 for binding to each said aminophospholipids (claim 6), wherein said antibody further binds to phosphatidylethanolamine (claim 7), wherein said antibody further binds to phosphatidylethanolamine and effectively competes with monoclonal antibody 3G4 for binding to phosphatidylethanolamine (claim 8), wherein said antibody is an IgM antibody (claim 12), wherein said antibody is an IgG antibody (claim 13), wherein said antibody is an antigen-binding fragment of an antibody, scFv, Fv, Fab', Fab, is camelized, single

domain, humanized, chimeric recombinant or engineered (claims 14-16, 19), wherein said antibody comprises an antigen binding region of said antibody operatively attached to a human antibody framework or constant region (claim 18), the composition of claim 1 wherein said composition is a pharmaceutically acceptable composition and is formulated for parenteral administration (claims 51 and 52), a composition comprising a purified anti-phosphatidylserine monoclonal antibody that binds to substantially the same epitope as 3G4 (claim 93), a composition comprising a purified monoclonal antibody that binds to phosphatidylserine and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidylserine (claim 94), a pharmaceutical composition comprising a pharmaceutically acceptable carrier and purified monoclonal antibody wherein said antibody binds to phosphatidylserine and effectively competes with 3G4 for binding to phosphatidylserine (claim 96), a purified monoclonal antibody that binds to phosphatidylserine and effectively competes with the monoclonal antibody 3G4 for binding to phosphatidylserine (claim 97), a hybridoma that produces a monoclonal antibody that effectively competes with 3G4 for binding to phosphatidylserine (claim 98), the composition of claim 1, 96, 97, 98 wherein said antibody binds to phospahtidylserine in combination with a protein cofactor (claim 100, 108, 113, 118), the antibody of claim 1, 96, 97, 98 wherein said antibody binds to PS in an ELISA with blocking buffer comprising 10% bovine serum (claims 101, 102, 109, 110, 114, 115, 119, 120), a composition comprising a purified monoclonal antibody that binds to phosphatidylserine and effectively competes with monoclonal antibody 3G4 for binding to phosphatidylserine (claim 122).

WO 00/02584 teaches monoclonal antibodies that bind phosphatidylserine (PS), and cross-react with other aminophospholipids. These monoclonal antibodies include IgG and IgM antibodies (PS3A, PSF6, PSF7, PSB4, PS3H1, PSE10, BA3B5C4, PS4A7, PS1G3, 3SB, PSC8, PSF11, PSG3, PSD11, PSF10, PS1B, PSD12, PS2C11 (p. 23, lines 15-28; p. 71, line 29 through p. 73, line 9; p. 68, entire section E2). As evidenced by Rote et al (Clinical immunology and Immunopathology, 1993, 66:193-200) and Umeda et al (J of Immunology, 1989, 143:2273-2279), both of which produced some of said monoclonal antibodies as taught by WO 00/02584, several monoclonal antibodies cross-react to bind to other aminophospholipids such as phosphatidic acid, phosphatidylinositol, phosphatidylglycerol, and cardiolipin, as set forth above. WO 00/02584 teaches that some of said monoclonal antibodies bind to phosphatidylethanolamine in addition to PS (PS3A, PSF6, PSF7, PSB4, PS3H1, and PS3E10) (p. 23, lines 15-22). WO 00/02584 teaches that the antibody can be an antibody fragment, scFv, Fv, Fab', Fab, chimeric, recombinant, or bispecific, or humanized antibodies that have antigen binding regions attached to human antibody framework or constant region (p. 102-104, section E10; p. 93-96, section E7; p. 100-102, section E9; p. 151, lines 2-10; p. 152, lines 1-5; p. 27, lines 7-15). WO 00/02584 teaches pharmaceutical compositions comprising the antibodies and the treatment of cancer using said antibodies for targeting tumor vasculature (p. 104, section F; p. 48-61, section C; p. 110-118, section H). WO 00/02584 teaches parenteral formulation (p. 104-107, section F1). WO 00/02584 teaches that anti-phospholipid antibodies recognize

phospholipids with protein cofactors (p. 82, lines 9-20; p. 83, lines 23-31). WO 00/02584 teaches hybridomas for producing monoclonal antibodies (p. 25-27).

The reference does not specifically teach that the antibody effectively competes with 3G4, binds substantially the same epitope as 3G4, or binds to PS in an ELISA that comprises blocking buffer comprising 10% bovine serum. However, the claimed monoclonal antibody appears to be the same as the prior art antibody, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. **A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s)**. See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761

(CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1-19, 23, 51, 52, and 93-122 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-37 of copending **Application No. 10/642,071**. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims of Application 10/642,071 are drawn to a method for treating an animal with cancer comprising administering a monoclonal antibody that binds to phosphatidylserine and effectively competes with antibody 3G4 for binding to phosphatidylserine or by administering antibody 3G4 itself, which anticipates the antibody in the pending claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

12. Claims 1-19, 23, 51, 52, and 93-122 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-36 and 39-57 of copending **Application No. 10/642,120**. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims of

Application 10/642,120 are drawn to a method for inhibiting virus replication or ongoing infection comprising using a monoclonal antibody that binds to phosphatidylserine and effectively competes with antibody 3G4 for binding to phosphatidylserine or by using antibody 3G4 itself, which anticipates the antibody in the pending claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. Claims 1-19, 23, 51, 52, and 93-122 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-34 of copending **Application No. 10/642,058.** Although the conflicting claims are not identical, they are not patentably distinct from each other because claims of Application 10/642,058 are drawn to a method for treating an animal with cancer comprising administering a monoclonal antibody that binds to phosphatidylserine and effectively competes with antibody 3G4 for binding to phosphatidylserine, which anticipates the antibody in the pending claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. Claims 1-19, 23, 51, 52, and 93-122 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-31 of copending **Application No. 10/642,116.** Although the conflicting claims are not identical, they are not patentably distinct from each other because claims of Application

10/642,116 are drawn to a composition comprising a monoclonal antibody that binds to phosphatidylserine and effectively competes with antibody 3G4 for binding to phosphatidylserine, which anticipates the antibody in the pending claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. Claims 1-19, 23, 51, 52, and 93-122 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-55 of copending **Application No. 10/642,119.** Although the conflicting claims are not identical, they are not patentably distinct from each other because claims of Application 10/642,119 are drawn to a method of inhibiting virus replication, spread, or ongoing infection comprising using an immunoconjugate comprising an antibody that binds to phosphatidylserine and effectively competes with antibody 3G4 for binding to phosphatidylserine or wherein the immunoconjugate comprises antibody 3G4, which anticipates the antibody in the pending claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

16. Claims 1-19, 23, 51, 52, and 93-122 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of copending **Application No. 10/642,065.** Although the conflicting claims are not identical, they are not patentably distinct from each other because claims of Application

10/642,065 are drawn to a method for treating an animal with cancer comprising administering an immunoconjugate comprising an antibody that binds to phosphatidylserine and effectively competes with antibody 3G4 for binding to phosphatidylserine, which anticipates the antibody in the pending claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

17. Claims 1-19, 23, 51, 52, and 93-122 are provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 of copending **Application No. 10/620,850.** Although the conflicting claims are not identical, they are not patentably distinct from each other because claims of Application 10/620,850 are drawn to a composition comprising monoclonal antibody 3G4, which anticipates the antibody in the pending claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Relevant arguments

Claim Rejections - 35 USC § 102

18. Applicants state that the rejection of new claim 122 under 102(b) as being anticipated by Maneta-Peyret et al (see section 6 above) would be *prima facie* improper because the claim recites a "purified" antibody and that Maneta-Peyret et al does not teach a purified antibody, but rather, a heterogeneous mixture of innumerable different antibodies (p. 33 of remarks).

The arguments has been considered but is not found persuasive because the term "purified" does not limit the antibody comprised in the composition to a single entity in its purist form. The specification does not provide a limiting definition of "purified". The antibody composition taught by Maneta-Peyret et al comprises an antibody that is isolated from its source, hence it is purified.

19. **Conclusion:** No claim is allowed. Applicants filed a terminal disclaimer to overcome the provisional double patenting rejection of claims over Applications 10/642,124; 10/642,122; 10/642,099; 10/642,060; 10/642,064; and 10/642,118. Applicants amended the claims to recite a "monoclonal" antibody to overcome the rejection of claims 1, 93, 94, and 97 under 102(b) as anticipated by Maneta-Peyret et al. The rejection of claims 51, 52, and 96 under 112 1st paragraph (section 4 of previous Office Action) is withdrawn in view of Applicants' arguments.

20. All other rejections recited in the Office Action mailed April 7, 2006 are hereby withdrawn.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura B. Goddard, Ph.D. whose telephone number is (571) 272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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